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(19) (CA) **APPLICATION FOR CANADIAN PATENT** (12)

(54) Methods for Inhibiting Uterine Fibrosis

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(57) 9 Claims

5,097,6/89

Notice: This application is as filed and may therefore contain an incomplete specification.



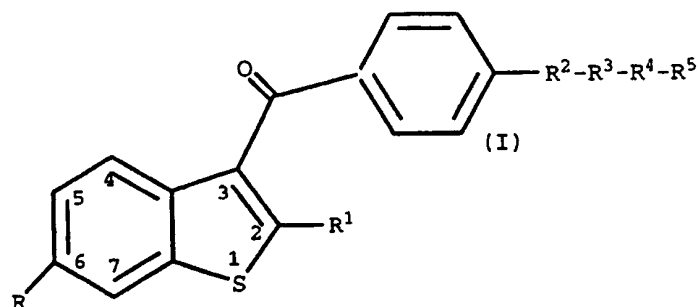
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ABSTRACT

A method of inhibiting uterine fibrosis
comprising administering to a human in need of treatment an
effective amount of a compound having the formula



wherein R is hydrogen; hydroxy; C₁-C₆ alkoxy; a
group of the formula -O-C(O)-R^a, wherein R^a is hydrogen, C₁-
C₆ alkyl optionally substituted with amino, halo, carbonyl,
C₁-C₆ alkoxy, carbonyl, C₁-C₇ alkanoyloxy, carbamoyl and/or
aryl; or R^a is C₁-C₆ alkenyl optionally substituted with
aryl; or R^a is a C₃-C₇ cycloalkyl; or R^a is aryl optionally
substituted with hydroxy, C₁-C₆ alkyl, C₁-C₆ alkoxy, and/or
halo; or R^a is -O-aryl, said aryl optionally substituted
with hydroxy C₁-C₆ alkyl, C₁-C₆ alkoxy, and/or halo,

or R is a group of the formula -O-SO₂-R^b wherein
R^b may be C₁-C₆ alkyl or aryl optionally substituted with
C₁-C₆ alkyl;

or R is carbamoyloxy wherein the nitrogen may be
substituted once or twice with C₁-C₆ alkyl;

or R is a group of the formula -O-C(O)R^c-O-(C₁-C₆
alkyl) wherein R^c is a bond or C₁-C₆ alkanediyl;

R¹ is halo, C₁-C₆ alkyl, C₁-C₇ alkyl substituted
with C₁-C₆ alkyl, substituted or unsubstituted C₃-C₇
cycloalkyl, or substituted or unsubstituted C₃-C₇
cycloalkenyl;

R² is O or CH₂;

R³ is CH₂ or (CH₂)₂;

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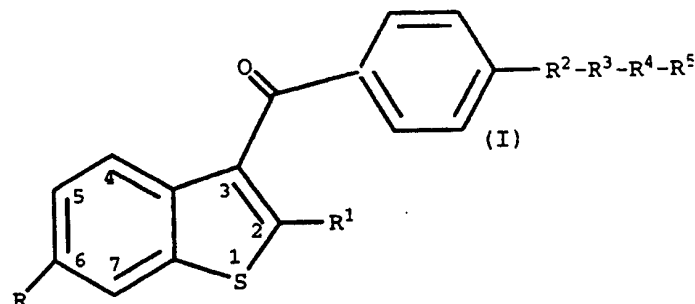
R⁴ is $\overset{\text{O}}{\parallel}\text{-C-}$, CH₂, or a bond; and

R⁵ is amino, nitrilo optionally substituted once or twice with C₁-C₆ alkyl; or an N-heterocyclic ring which optionally has another hetero atom selected from N, O, or S
5 in said ring; or a pharmaceutically acceptable salt or solvate thereof.

We claim:

1. A compound having the formula

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wherein R is hydrogen; hydroxy; C₁-C₆ alkoxy;
 a group of the formula -O-C(O)-R^a, wherein R^a is
 10 hydrogen, C₁-C₆ alkyl optionally substituted with amino,
 halo, carbonyl, C₁-C₆ alkoxy, carbonyl, C₁-C₇ alkanoyloxy,
 carbamoyl and/or aryl; or R^a is C₁-C₆ alkenyl optionally
 substituted with aryl; or R^a is a C₃-C₇ cycloalkyl; or R^a
 is aryl optionally substituted with hydroxy, C₁-C₆
 15 alkyl, C₁-C₆ alkoxy, and/or halo; or R^a is -O-aryl, said
 aryl optionally substituted with hydroxy C₁-C₆ alkyl, C₁-
 C₆ alkoxy, and/or halo,

or R is a group of the formula -O-SO₂-R^b
 wherein R^b may be C₁-C₆ alkyl or aryl optionally
 20 substituted with C₁-C₆ alkyl;

or R is carbamoyloxy wherein the nitrogen may
 be substituted once or twice with C₁-C₆ alkyl;

or R is a group of the formula -O-C(O)R^c-O-
 (C₁-C₆ alkyl) wherein R^c is a bond or C₁-C₆ alkanediyl;

25 R¹ is halo, C₁-C₆ alkyl, C₁-C₇ alkyl
 substituted with C₁-C₆ alkyl, substituted or
 unsubstituted C₃-C₇ cycloalkyl, or substituted or

unsubstituted C₃-C₇ cycloalkenyl;

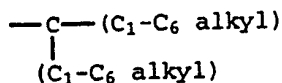
R² is O or CH₂;

R³ is CH₂ or (CH₂)₂;

R⁴ is $\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}- \end{array}$, CH₂, or a bond; and

5 R⁵ is amino, nitrilo optionally substituted
once or twice with C₁-C₆ alkyl; or an N-heterocyclic
ring which optionally has another hetero atom selected
from N, O, or S in said ring; or a pharmaceutically
acceptable salt or solvate thereof, for use in
10 inhibiting uterine fibrosis.

2. A compound according to Claim 1 wherein R¹ is
a group having the formula



15 or a cycloalkyl group with a carbon number of three to
eight that may be substituted with C₁-C₆ alkyl or hydroxy.

3. A compound of Claim 2 wherein R is hydroxy.

20

4. A compound according to Claim 3 wherein R² is
O and R⁴ is CH₂.

25 5. A compound according to Claim 1 wherein said
compound is (6-hydroxy-2-cyclohexylbenzo[b]thien-3-yl)[4-
[2-(1-pyrrolidinyl)ethoxy]phenyl]methanone, (6-hydroxy-2-
cyclohexylbenzo[b]thien-3-yl)[4-[2-(1-
piperidinyl)ethoxy]phenyl]methanone, (6-hydroxy-2-
cycloheptylbenzo[b]thien-3-yl)[4-[2-(1-
30 pyrrolidinyl)ethoxy]phenyl]methanone, (6-hydroxy-2-
cycloheptylbenzo[b]thien-3-yl)[4-[2-(1-

piperidinyl)ethoxy]phenyl]methanone, (6-hydroxy-2-isopropylbenzo[b]thien-3-yl)[4-[2-(1-pyrrolidinyl)ethoxy]phenyl]methanone, (6-hydroxy-2-isopropylbenzo[b]thien-3-yl)[4-[2-(1-piperidinyl)ethoxy]phenyl]methanone.

6. A compound according to Claim 3 wherein R² is CH₂.

7. A compound according to Claim 6 wherein said compound is (6-hydroxy-2-cyclohexylbenzo[b]thien-3-yl)[4-[3-(1-pyrrolidinyl)propyl]phenyl]methanone, (6-hydroxy-2-cyclohexylbenzo[b]thien-3-yl)[4-[3-(1-piperidinyl)propyl]phenyl]methanone, or (6-hydroxy-2-cyclohexylbenzo[b]thien-3-yl)[4-[2-(1-pyrrolidinylcarbonyl)ethyl]phenyl]methanone.

8. A compound according to Claim 2 wherein R is C₁-C₆ alkoxy.

9. A compound according to Claim 8, wherein said compound is (6-methoxy-2-cyclohexylbenzo[b]thien-3-yl)[4-[2-(1-piperidinyl)ethoxy]phenyl]methanone or (6-acetoxy-2-cyclohexylbenzo[b]thien-3-yl)[4-[2-(1-piperidinyl)ethoxy]phenyl]methanone.

SUBSTITUTE

REMPLACEMENT

SECTION is not Present

Cette Section est Absente